PERINATAL LESSONS FROM THE PAST

Perinatal lessons from the past: Sir Norman Gregg, ChM, MC, of Sydney (1892–1966) and rubella embryopathy

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By identifying rubella infection in early pregnancy as a cause of congenital malformations and disabilities, Gregg alerted the medical profession to the importance of the prenatal environment.

Norman McAlister Gregg was born in Burwood, Sydney, on 7 March 1892.[1] He was the sixth child of James and Mary Gregg. After attending Homebrush Grammar School, he entered Sydney Grammar School in 1906. There, he proved to be both an outstanding scholar and an all-round athlete and cricketer. On winning the State's Barker Scholarship to the University of Sydney, he studied medicine, graduating in 1915 with first class honours. Meanwhile, he played cricket, tennis (winning the inter-university tennis doubles championship in 1914) and baseball for the university. He also became president of the Undergraduates' Association and a director of the University Union.

On qualifying in medicine, Gregg immediately left Australia to join the British Expeditionary Force in France as a captain in the Royal Army Medical Corps. There he was wounded, and in 1917 won the Military Cross for gallantry in the field. After demobilisation in 1919, he returned to Sydney to take up a resident appointment at the Royal Prince Alfred Hospital. Then in 1922, he returned to England to study ophthalmology, first in London and afterwards in Birmingham. Back in Australia in 1923, he quickly established himself as an ophthalmic surgeon in private practice, in addition to which he held honorary appointments at the Royal Prince Alfred Hospital and the Royal Alexandra Hospital for Children. It was at this time that he married Miss Haidee Carson. They had two daughters and 42 years of happy life together.

By 1941, Gregg had become senior ophthalmic surgeon to both the Royal Prince Alfred Hospital and the Royal Alexandra Hospital for Children, and was also lecturer in ophthalmology at the University of Sydney. Besides having a busy private practice and much committee work, he had also become captain of his golf club and was later to become its president (fig 1). In the same year, he published his seminal and ground-breaking paper on the effects of rubella on the developing fetus in early pregnancy.

Rubella, derived from the Latin ''little red'', was recognised in 1814 in Germany as a mild illness characterised by a rash, adenopathy and fever. At first, the condition was thought to be a variant of measles. Although a viral aetiology was suspected as early as 1914, the virus was itself not isolated until 1961. Meanwhile, in 1940, there was a severe rubella epidemic in Australia, and the following year Gregg reported[2] the occurrence of congenital cataracts among 78 infants, 68 of whom were born to mothers who had had this infection early in pregnancy. The appearance of the cataracts was unusual as they affected all but the outermost layers of the lens. This led Gregg to suggest that the cataractous process had begun early in the life of the embryo. He wrote:

> ''Although one was struck with the unusual appearance of the cataracts in the first few cases, it was only when similar cases continued to appear that serious thought was given to causation. The remarkable similarity of the opacities in the lens, the frequency of an accompanying affection of the heart and the widespread geographical incidence of the cases suggested there was some common factor in the production of the diseased condition, and suggested it was the result of some constitutional condition of toxic or infective nature rather than of a purely development defect.''[2]

In his paper, Gregg stated that ''maternal rubella infection in early pregnancy was the cause of the babies' defects.'' Later in 1943, he[3] and others added deafness to cataracts and congenital heart disease in what became known as the triad of congenital rubella embryopathy. Mental retardation was also recognised as part of the syndrome. Later, thrombocytopenic purpura, hepatitis, bone lesions and meningoencephalitis were recognised as manifestations of the disease.

In the 1940s, there was a widespread prejudice throughout the medical profession in the belief that all congenital malformations were inherited. It was considered unscientific to include non-genetic factors.[4] Although Gregg's work drawing attention to the prenatal environment was cautiously welcomed in Australia, it was several years before it received the recognition it deserved abroad. In 1944, Gregg was awarded the Australian Shorney Prize for ophthalmology. Then after a gap of 7 years, the University of Toronto conferred on him the Charles Mickle Fellowship. Thereafter, honours came rapidly: the James Cook Medal of the Royal Society of New South Wales; the Addingham Medal of the University of Leeds; fellowship of the Royal College of Obstericians and Gyanecologists *ad*

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Figure 1 Sir Norman Gregg (1892–1966).

eundem in 1952; fellowship of the Royal Australasian College of Physicians; honorary doctorates of the Universities of Melbourne and of Sydney, and of the Australian National University; and honorary fellowships of the American Academy of Ophthalmology and Otolaryngology, and of the Australian Paediatric Association. In 1953, he was knighted by Her Majesty the Queen for his services to medicine. Later, in 1963, he was elected a fellow of the Australian Postgraduate Federation in Medicine and the following year received, with Dr Kate Campbell of Melbourne, the first Britannica Australia Award in Medicine for an outstanding contribution to research regarding the vulnerability of unborn children. Norman Gregg's achievements continued. He became president of the Ophthalmological Society of Australia and also of the Royal Alexandra Hospital for Children. He was very active in establishing the Ophthalmic Research Institute of Australia and in supporting the Children's Medical Research Foundation. In addition, he was the first chairman of the Advisory Board of Modern Medicine in Australia and president of the second congress of the Asia-Pacific Academy of Ophthalmology.[1]

To complete the rubella story, the virus (RNA togavirus, genus rubivirus) was isolated in 1961. By 1969, a live attenuated rubella virus vaccine had been developed and licensed, since which time vaccination programmes during childhood have largely eliminated this cause of congenital malformation and disability from the populations covered. The significance of this advance may be appreciated when it is recollected that there were no fewer than 20 000 cases of congenital cataract in the US after the 1964–5 epidemic of rubella and that before vaccination this infection was responsible for 40% of all cases of congenital deafness.

Sir Lorimer Dods, to whose obituary tribute this account is much indebted,[1] described Gregg as a tall, lithe and vigorous man, dedicated to his patients, and with an exciting and stimulating approach to clinical problems. His enthusiasm was infectious. He never spared himself and, while having little time for fools and slackers, was always ready to encourage younger men. He has been described as an inspiring and clear thinking leader who was held in great respect and affection by all. Despite the many honours heaped on him, he retained ''a natural humility, and remained a simple, uncomplicated person with a special love for his home and many friends—a most sympathetic and understanding man of impeccable integrity and unceasing devotion to duty''. After retirement he lived with his wife and two daughters for the remaining 14 years of his life in his home at Woolahra. There he died peacefully in his sleep in 1966, at the age of 74.

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